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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/974,973	10/12/2001	Paul D. Hanke	1533.1230001/MAC/RGM	8115

28393 7590 04/22/2003

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EXAMINER	
SLOBODYANSKY, ELIZABETH	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 04/22/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No.	Applicant(s)	
	09/974,973	HANKE, PAUL D.	
	Examin r	Art Unit	
	Elizabeth Slobodyansky	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *9-11 and 14-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-8,12,13,19 and 20* is/are rejected.

7)☒ Claim(s) *3 and 4* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 May 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

Claims 1-20 are pending.

Election/Restriction

Applicant's election with traverse of Group I, claims 1-3, 5-8, 12, 13, 19 and 20, drawn to a DNA encoding SEQ ID NO:2, in Paper No. 15 filed March 14, 2003 is acknowledged. The traversal is on the ground(s) that "the Examiner alleges that the groups I-V are patentably distinct inventions. However, even if patentably distinct inventions appear in a single application, restriction remains improper unless the Examiner can also show that the search and examination of the groups would entail a "serious burden". It is only where the inventions are independent, that the "serious burden" is inherent and need not be explained by the Examiner (*see* MPEP § 803 and 808) (Remarks, page 1).

The examiner notes that in view of the identity of SEQ ID NOs:1 and 3, and SEQ ID NOs:2 and 4, Group I is rejoined with Group II and Group IV is rejoined with Group V. There was no way of knowing that said sequences are identical at the time the restriction requirement was made. This issue is addressed below.

Applicants further argue that "With respect to Groups I, II and IV, V, Applicants submit that a search of either the nucleotide sequence or polypeptide claims would provide useful information for the remaining claims" (paragraph bridging pages 1 and

2). This is not found persuasive because proteins and nucleic acids are different compounds each with its own chemical structure and function, and they have different utilities. A DNA molecule can be used for the production of an encoded enzyme and as a hybridization probe. An enzyme can be obtained by a materially different method such as by the biochemical purification. Furthermore, the examination of nucleic acids with proteins would require diverse considerations.

Applicants further argue that Groups I, II, IV and V should be rejoined with Group III due to lack of "serous burden" (page 2). This is not persuasive because Invention III is patentably distinct from inventions I, II, IV and V because it is drawn to methods of making of a product, an amino acid, that is neither used nor produced by inventions I, II, IV and V. Further, amino acids can be produced not only by methods of invention III but also by chemical synthesis, for example.

The requirement is still deemed proper and is therefore made FINAL.

Claims 9-11 and 14-18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Groups III-V, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 15.

Drawings

The proposed drawing correction of Figure 2 filed on May 10, 2002 has been disapproved because it is not in the form of a pen-and-ink sketch showing changes in red ink or with the changes otherwise highlighted. See MPEP § 608.02(v).

Specification

The instant disclosure contains sequence disclosure that is encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825. 37 CFR 1.821(c) requires the use of an assigned sequence identifier for each sequence. In the instant application the same sequences are assigned different sequence identifiers such as SEQ ID NOs:1 and 3 and SEQ ID NOs:2 and 4, respectively, for a single nucleotide and amino acid sequence.

Applicants are required to submit a substitute corrected Sequence Listing and a computer readable form thereof accompanied by the amendment to the specification and Figures.

The disclosure is objected to because it is unclear what "BF100" stands for in Table 2, page 22 and at Figures 4-6, for example.

Applicants are requested to indicate to which residues in SEQ ID NO:19, the sequences of SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16 and SEQ ID NO:18 correspond.

Claim Objections

Claim 19 is objected to as dependent from non-elected claim 18. Despite this problem claim 19 was treated as if it were properly written, i.e. as if it included all limitations of claim 18, in the interests of compact prosecution.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in

scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Applicant is advised that should claim 3 be found allowable, claim 4 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). In the instant case, both claims are drawn to the same nucleotide sequence.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5-8, 12, 13, 19 and 20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1, with dependent claims 5-8, 12 and 13, is directed to a DNA encoding a mutant pyruvate carboxylase that is desensitized to feedback inhibition by aspartic acid, said mutant pyruvate carboxylase having an amino acid sequence containing at least one mutation selected from the group consisting of seven specific mutations in SEQ ID NO:19. Since the number of allowed mutations is not limited in terms of the mutant's sequence homology to SEQ ID NO:19, this amounts to any structure.

The specific recited mutations constitute less than 1% of the entire SEQ ID NO:19 that is 1140 amino acid long.

The specification does not contain any disclosure of the structures of all mutant pyruvate carboxylases containing the specific mutations that are desensitized to feed back inhibition by aspartic acid. The genus of proteins that comprise these molecules is a large variable genus comprising many structurally diverse proteins. The specification discloses only a single species of the claimed genus, a mutant pyruvate carboxylase comprising all seven specific mutations and having the amino acid sequence of SEQ ID NO:2. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the "functionality" of being "desensitized to feed back inhibition by aspartic acid" and fails to provide any structure: function correlation present in all members of the claimed genus. Therefore, the specification is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art

cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 19 and 20 are directed to DNAs encoding a genus of polypeptides of any structure and function comprising SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16 or SEQ ID NO:18. Said sequences are 13-18 amino acids in length. The specification does not contain any disclosure of the function of all DNA sequences encoding polypeptides that comprise SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16 or SEQ ID NO:18. The genus of DNAs that comprise these above DNA molecules is a large variable genus with the potentiality of encoding many different proteins. The genus of claimed DNAs encodes polypeptides retaining the requisite pyruvate carboxylase activity and polypeptides of unknown function. Therefore, many functionally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. One skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 1, 5-8, 12, 13, 19 and 20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA encoding SEQ ID NO:2, does not reasonably provide enablement for a DNA encoding a mutant pyruvate carboxylase that is desensitized to feedback inhibition by aspartic acid, said mutant pyruvate carboxylase having an amino acid sequence of unknown homology to SEQ ID NO:19 containing at least one (or seven) specific mutations or a specific fragment . It does not reasonably provide enablement for a DNA encoding a polypeptide of unknown function having an amino acid sequence of unknown homology to SEQ ID NO:19 containing a specific fragment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7)considered in determining whether undue experimentation is required, are summarized the predictability or unpredictability of the art, and (8) the breadth of the claims.

Factors pertinent to this discussion include predictability of the art, guidance in the specification, breadth of claims, and the amount of experimentation that would be necessary to use the invention.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of mutants broadly encompassed by the claims, *supra*.

The specification teaches a DNA of SEQ ID NO:1 that encods a mutant pyruvate carboxylase with seven specific mutations relative to the wild-type sequence of SEQ ID NO:19. The specification does not teach any pyruvate carboxylase mutants that comprise in addition to the requisite mutations additional mutations and exhibit the requisite property. Further, it fails to provide information regarding other combinations of substitute amino acids that would result in a mutant with the requisite characteristics. While there is a great number of possible mutants, it is *a priori* unpredictable as to which mutant will exhibit the claimed property. Therefore, the breadth of these claims is much larger than the scope enabled by the specification.

The amino acid sequence of a protein determines its structural and functional properties, and predictability of what changes in the amino acid sequence can be tolerated and result in similar activity is extremely complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's structure from mere sequence data are limited. Furthermore, while recombinant techniques are

available, it is not routine in the art to screen large numbers of peptide mutants where the expectation of obtaining similar activity is unpredictable based on the instant disclosure. Therefore, one of ordinary skill would require guidance, such as information regarding the specific amino acid changes that would render a pyruvate carboxylase desensitized to feedback inhibition by aspartic acid, in order to make a mutant pyruvate carboxylase with the requisite property other than a mutant pyruvate carboxylase of SEQ ID NO:2 in a manner reasonably correlated with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

Furthermore, claims 19 and 20 encompass DNAs encoding polypeptides of unknown function in addition to polypeptides with the requisite pyruvate carboxylase activity. It would require undue experimentation to establish the function of all polypeptides comprising the recited fragments. Without knowing the function of a polypeptide, it is impossible to know how to use it and a DNA encoding thereof.

Claim 2 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the DNA contained in Deposit Number NRRL B-30293 is required to practice the claimed invention. As a required element it/they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it/they is/are not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the microorganism(s). See 37 C.F.R. § 1.802.

The specification discloses that the deposit was made on May 30, 2000 (page 6). However, it is not apparent if the microorganism(s) are readily available to the public.

Since it appears that the deposit(s) has/have been made under the terms of the Budapest Treaty, an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his/her signature, and registration number, stating that the specific strain(s) has/have been deposited under the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 C.F.R. § 1.808.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 5-8, 12 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, with dependent claims 5-8, 12 and 13, is confusing as it is unclear that it drawn to a DNA encoding a mutant pyruvate carboxylase with the requisite property having an amino acid sequence that differs from the wild-type sequence of SEQ ID NO:19. Furthermore, since the specification consistently uses the term "feed-back resistant", the term "desensitizes" in claim 1 renders the claim unclear.

Claim 2 is confusing as reciting different fragments of the same sequence under different SEQ ID Nos. Furthermore, the term "complementary" can mean different degree of complementarily rendering the metes and bound of the claim unascertainable.

Allowable Subject Matter

Claim 3 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is

(703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner

April 15, 2003